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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/619,754

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Birgit Bossenmaier

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35489

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02/04/2010

Arnold & Porter LLP (24126)

Attn: IP Docketing Dept.

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EXAMINER

HOLLERAN, ANNE L

ART UNIT

PAPER NUMBER

1643

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/619,754	<b>Applicant(s)</b> BOSSENMAIER ET AL.	
	<b>Examiner</b> ANNE L. HOLLERAN	<b>Art Unit</b> 1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 13 November 2009.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 23-28, 40-52 and 64-73 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 23-28, 40, 42-52 and 64-73 is/are rejected.
- 7) ☒ Claim(s) 41 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>11/13/2009</u> .  | 6) <input type="checkbox"/> Other: _____                          |

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### **DETAILED ACTION**

The amendment filed 11/13/2009 is acknowledged. Claims 23-28, 40-52 and 64-73 are pending and examined on the merits.

#### ***Claim Rejections Withdrawn:***

#### ***Claim Rejections - 35 USC § 112***

The rejection of claims 23-28, 40-52, 64-73 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the amendment to claims 23, 42, 47 and 71.

#### ***Claim Rejections Maintained:***

#### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 47-52, 64, and 66-70 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Sliwkowski (US 6,949,245; issued Sep. 27, 2005; effective filing date is June 25, 1999) in view of Bangalore (Bangalore, L., et al. Proc. Natl. Acad. Sci, USA, 89: 11637-11641, 1992) or DiGiovanna (supra).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the

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inventor of this application and is thus not an invention “by another”; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Applicants’ arguments have been carefully considered, but fail to persuade. Applicants assert that the combination of Sliwkowski with Bangalore has no teaching whatsoever about using the detection of ErbB receptor phosphorylation as a means to predict patient response to cancer treatment, in particular treatment with an antibody inhibiting the association of Her2 with another member of the ErbB receptor family. Applicants assert that while DiGiovanna suggests in generic terms that detecting the phosphorylation of the p185 receptor might be used to predict responses to anti-p185 immunotherapy, that DiGiovanna provides absolutely no evidence that this would be the case or that this tentative suggestion might apply to the type of antibodies which inhibit the association of Her2 with another member of the ErbB receptor family. The examiner disagrees with applicants conclusion that the combination of Sliwkowski with Bangalore or diGiovannana does not make obvious the claimed invention because Sliwkowski teaches a method of treating a subject with cancer that may be characterized as having excessive

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activation, where the treatment is the administration of an antibody such as the 2C4 antibody.

Therefore the suggestion to test for receptor activation comes from Sliwkowski because Sliwkowski suggests this population of cancer patients. Both Bangalore and DiGiovanna teach that phosphorylation of ErbB2 is a measure of ErbB2 activation. Therefore, it would have been obvious at the time the invention was made to combine Sliwkowski with either Bangalore or DiGiovanna to make the claimed inventions.

Claims 47-52, and 65-73 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Sliwkowski (US 6,949,245; issued Sep. 27, 2005; effective filing date is June. 25, 1999) in view of Bangalore (Bangalore, L., et al. Proc. Natl. Acad. Sci, USA, 89: 11637-11641, 1992) or DiGiovanna (supra), and further in view of Terstappen (US 6,365,362).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in

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accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Applicants' arguments have been carefully considered, but fail to persuade. Applicants state that the claims are not rendered obvious by the combination of Sliwkowski and Bangalore, or Sliwkowski and DiGiovanna, and that the addition of Terstappen does not change this outcome. However, as discussed above in the previous rejection, the teachings of Sliwkowski and Bangalore, or of Sliwkowski and DiGiovanna provide motivation to combine the cited references, and the combinations of the references teach all of the limitations of the claims cited in the previous rejection. Terstappen is cited in the present rejection to teach limitations having to do with assaying carcinoma cells in the blood, which may be used to monitor patients for response to therapy. Terstappen is not required for the previous rejection. Therefore, applicants' arguments are not found persuasive.

Claims 23-28, 40 and 42-45 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Bangalore (supra) in view of DiGiovanna (supra), and further in view of Lewis (Lewis, G. D., et al., Cancer Research, 56: 1457-1465, 1996) for the reasons of record.

Applicants' arguments have been carefully considered, but fail to persuade. Applicants state that Bangalore and DiGiovanna, when taken alone or in combination, do not teach a method of identifying a Her2 positive tumor as responsive to treatment with an antibody inhibiting the

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association with another member of the ErbB receptor family based on phosphorylation of the Her2 receptor with a reasonable expectation of success; and that Lewis does not correct this deficiency. This is not persuasive because Bangalore and DiGiovanna teach that phosphorylation of Her2 is a measure of Her2 activation, DiGiovanna states that using a phosphorylation assay may be useful to test anti-Her2 antibodies. Because Lewis teaches that the mechanism by which 2C4 inhibits Her2 activity is to inhibit activation of Her2 by heregulin, the motivation to treat tumor cells with the 2C4 antibody or the rhuMab 2C4 is to test whether a specific cancer cell type expresses an activated Her2 in the presence of heregulin, and whether such tumor cells respond to the 2C4 antibody or to rhuMab 2C4 when treated with either of these antibodies. Therefore, applicants' arguments are not found persuasive.

### ***Conclusion***

Claim 41 is objected to for depending from a rejected claim.

Please note: NO deposit rejection is required for claims reciting rhuMab 2C4, because the complete structure of this antibody is provided on page 26 of the specification.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO**

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MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne Holleran, whose telephone number is (571) 272-0833. The examiner can normally be reached on Monday through Friday from 9:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached on (571) 272-0832. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Official Fax number for Group 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

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system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private

PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Anne L. Holleran

Patent Examiner

/Alana M. Harris, Ph.D./

Primary Examiner, Art Unit 1643